

ROHM
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HAAS
COMPANY

(A)

July 27, 1992

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Document Processing Center (TS-790)
Office of Toxic Substances
Attn: Section 8(e) Coordinator (CAP Agreement)
Environmental Protection Agency
401 M Street, S.W.
Washington, DC 20460

Dear Sir or Madam:

Re: 8(e) CAP-0103; Data Submission

The enclosed document is submitted pursuant to the TSCA Section 8(e) Compliance Audit Program and the CAP Agreement between Rohm and Haas Company and the Environmental Protection Agency. This document does not contain confidential business information.

The following is a summary of the contents of the submission under Unit II.C.3 of the CAP Agreement:

Tested Chemical:

Propionic acid, 2-[5-(2-chloro-4-(trifluoromethyl)-phenoxy)-2-nitrophenoxy]-, ethyl ester
50594-49-5

CASRN:

Title of Report or Study:

RH-5205: Twenty-four month Oral Safety Evaluation study in rats (Report No. 81RC-1007)
Unusual toxicological effect on bone marrow.

Reportable Effect:

If additional information is required, please contact the undersigned at (215) 592-3139.
Thank you.

Sincerely,

Ronald L. Keener, Ph.D.
Regulatory Affairs Director
Product Integrity Department

RLK:so
Enclosure

mm
07/95

E. M. Beavers
W. T. Lynch
S. J. Talucci
W. H. Watanabe
R. Y. Yih
TD Central File ✓

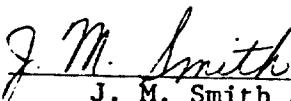
JMS-78-102

Spring House, July 7, 1978

To: Mr. V. H. Unger
From: J. M. Smith
Subject: RH-5205 - Mouse Chronic/Oncogenic Study

Attached is W. Lynch's preliminary tabulation of liver nodules and masses observed in mice fed diets containing RH-5205 for approximately 2 years. This tabulation demonstrates a significant increase in liver nodules and masses in the low and middle dose groups (0.5 and 1.6 ppm respectively).

In my opinion this finding, the marked effect upon the hemopoietic system and the absence of a no effect level at the lowest dose tested (0.5 ppm) in the mouse plus the effect upon the hemopoietic system in the rat at low doses demonstrate a high intrinsic toxicity of RH-5205 for rodents. While with time and expenditure of several hundred thousand dollars we might be able to demonstrate that these effects are specific for the rodent and that RH-5205 represents minimal hazard to man, I think toxicologically our chances for registration are very poor, i.e., less than 20%. Therefore, I recommend that toxicological evaluation of RH-5205 for purposes of registration be terminated.


J. M. Smith
J. M. Smith *bad*

JMS/bad

Attachment

RH-5205 - Mouse Oncogenicity

Group mg/kg ppm	I		II		III		IV		V	
	M	F	M	F	M	F	M	F	M	F
Mortality 1-3 mo.	0	1	1	0	0	0	0	2	16 ^b	7
3 mo. sacrifice	10	10	10	10	10	10	10	10	10	10
4-12 mo.	5	9	6	9	6	8	8	4	8	11
12 mo. sacrifice	10	10	10	10	10	10	10	10	10	10
13-24 mo.	24 ^a	26	27	23	27	26	26	27	25	29
24 mo. sacrifice	29	24	26	28	27	26	26	27	10	13
Total Number	78	80	80	80	80	80	80	80	79	80
 Liver Nod or Mass										
1-3 mo.										
3 mo. sacrifice										
4-12 mo.										
12 mo. sacrifice										
13-24 mo.	5	1	4	0	15	8	14	4	10	2
24 mo. sacrifice	5	4	6	2	19	11	20	12	3	7
Total	10	5	10	2	34	19	34	16	13	9
% 13-24 mo.	20.8	3.8	14.8	0	55.6	30.8	53.8	14.8	40.0	6.9
24 mo. sacrifice	17.2	16.7	23.1	7.1	70.4	42.3	76.9	44.4	30.0	53.8
Total	18.9	10.0	18.9	3.9	63.0	36.5	65.4	29.6	37.1	21.4

^aTwo post mortem sheets not received.

^bOne post mortem sheet not received.

RH-5205
100

RESEARCH
PATHOLOGY
SERVICES, INC.

May 10, 1981

William J. Lynch, Ph.D.
Toxicology Department
Rohm and Haas Company
McKean and Norristown Roads
Spring House, Pa. 19479

ROHM AND HAAS COMPANY
TOXICOLOGY DEPARTMENT ARCHIVES

RECEIVED: JUN 11 1982

ENTERED BY: EAJ

SUBJECT: RH-6201 and RH-5205: Twenty-four-Month Oral Safety Evaluation Study in Rats. Protocol No. DR-76-3. Histopathologic Evaluation of the Bone Marrow from Control and RH-5205-Treated Rats.

81RC-1007

Microscopic examination was made of hematoxylin-and-eosin-stained sections of bone with bone marrow from rats used in a chronic safety evaluation study on RH-6201 and RH-5205. This report includes only the microscopic findings in the bone marrow of the control rats and rats treated with RH-5205 that were necropsied after 67 days, 80 days, 90 days, and 12 months of treatment. The number of rats and dosage groups according to necropsy interval for which hematoxylin-and-eosin-stained sections were available for microscopic examination are listed in Tables 1, 2, 3, and 4, inclusive. The description of the histomorphologic findings for each rat of the various dosage groups for the four necropsy intervals are presented in Appendices I-IV, inclusive.

Microscopic examination of the bone marrow sections of the control and high dose rats necropsied after 67 days of treatment revealed an increased incidence and severity (up to marked) of hyperplasia of the bone marrow in the male high dose rats necropsied after this period of treatment. Two of these male rats also had focal myelosclerosis (Table 1). Similar treatment-related hyperplasia and focal myelosclerosis occurred in the high-mid dose male rats necropsied after 80 days of treatment (Table 2). Bone marrow sections from female rats from these necropsy intervals were not available for examination.

After 90 days of treatment, there was an increased incidence of rats with a moderate to marked bone marrow hyperplasia in male and female high dose rats that were available for microscopic examination. Myelosclerosis was not seen in any of these rats (Table 3). The bone marrow sections of the high-mid dose rats that were submitted for microscopic examination from the 12-month necropsy also showed a minimal increased incidence of bone marrow hyperplasia in the treated rats, as compared to the controls (Table 4) and as compared to rats at the same dosage level necropsied after 80 days of treatment. Myelosclerosis also was not seen in any of the rats necropsied after 12 months of treatment.

The increased incidence and severity of bone marrow hyperplasia and focal myelosclerosis was of sufficient degree in the RH-5205-treated rats to be considered a treatment effect. The type and extent of the bone marrow hyperplasia and myelosclerosis in the RH-5205-treated rats are comparable in extent and morphology to that seen in bone marrow sections of rats of the three-month toxicity study on RH-50,043 in rats (Protocol No. 80P-265).

W. Ray Brown

W. Ray Brown, D.V.M., Ph.D.
Veterinary Pathologist

WRB:kwh

Attachments

(

RHT 5205

2 Year Rat *

DOSING SCHEDULE

H Rats each group	Group	Sep	weeks		Dietary Concentration (ppm)				
			1,2	3,4	29-67	67-79	79-88 (90)	90+	
75	I A	Cont	M+F	0	0	0	0	0	0
75	I B	Cont	M+F	0	0	0	0	c	0
75	XI	low	M+F	1	10.4	2	2	2	2
75	VII	low-mid	M+F	31.5	44.5	63	63	63	63
75	VIII	high-mid	M	10	14.1	20	20	0	11.9
			F	10	14.1	20	20	20	20
15	IX	high	M	31.5	44.5	63	0	0	-
			F	31.5	44.5	63	63	63	-

- all sac. at 90 days.

W.T. Lynch

Study conducted at Pawson Research - Study was run for 2 years but histopath was not done. Rats examined at 67 days from high dose group (males) were: 3 found dead and 7 sacrificed. Remaining 5 males were put on control diet until 90d sac. 13 male high mid sac on day 79. Remaining males put on control diet for 9 days then on 11.9 ppm from day 90 on.

W.T. Lynch

Table 1. RH-6201 and RH-5205: Twenty-four-Month Oral Safety Evaluation Study in Rats. Protocol No. DR-76-3. Incidence of Histomorphologic Observations in the Bone Marrow of Control and RH-5205-Treated Rats - 67-Day Necropsy.

Dose Group*:	IA	IB	VIII	IX	IA	IB	VIII	IX
Sex:	M	M	M	M	F	F	F	F
Rats/Group Examined:	0	5	0	10	0	0	0	0
BONE MARROW:								
NO. EXAMINED	0	5	0	10	0	0	0	0
NO. NORMAL	0	3	0	0	0	0	0	0
-bone marrow hyperplasia,								
very slight	0	1	0	0	0	0	0	0
moderate	0	1	0	4	0	0	0	0
marked	0	0	0	6	0	0	0	0
-focal myelosclerosis	0	0	0	2	0	0	0	0

Table 2. RH-6201 and RH-5205: Twenty-four-Month Oral Safety Evaluation Study in Rats. Protocol No. DR-76-3. Incidence of Histomorphologic Observations in the Bone Marrow of Control and RH-5205-Treated Rats - 80-Day Necropsy.

Dose Group*:	IA	IB	VIII	IX	IA	IB	VIII	IX
Sex:	M	M	M	M	F	F	F	F
Rats/Group Examined:	0	5	13	0	0	0	0	0
BONE MARROW:								
NO. EXAMINED	0	5	13	0	0	0	0	0
NO. NORMAL	0	4	1	0	0	0	0	0
-bone marrow hyperplasia,								
very slight	0	1	0	0	0	0	0	0
slight	0	0	3	0	0	0	0	0
moderate	0	0	9	0	0	0	0	0
-focal myelosclerosis	0	0	1	0	0	0	0	0

*Group IA = Control
Group IB = Control

Group VIII = High-Mid Dose
Group IX = High Dose

Table 3. RH-6201 and RH-5205: Twenty-four-Month Oral Safety Evaluation Study in Rats. Protocol No. DR-76-3. Incidence of Histomorphologic Observations in the Bone Marrow of Control and RH-5205-Treated Rats - 90-Day Necropsy.

Dose Group*:	IA	IB	VIII	IX	IA	IB	VIII	IX
Sex:	M	M	M	M	F	F	F	F
Rats/Group Examined:	10	5	0	6	10	10	0	9
BONE MARROW:								
NO. EXAMINED	10	5	0	6	10	10	0	9
NO. NORMAL	8	4	0	0	7	7	0	2
-bone marrow hyperplasia,								
very slight	0	1	0	0	2	2	0	3
slight	1	0	0	1	1	1	0	1
moderate	1	0	0	4	0	0	0	3
marked	0	0	0	1	0	0	0	0

Table 4. RH-6201 and RH-5205: Twenty-four-Month Oral Safety Evaluation Study in Rats. Protocol No. DR-76-3. Incidence of Histomorphologic Observations in the Bone Marrow from Control and RH-5205-Treated Rats - 12-Month Necropsy.

Dose Group*:	IA	IB	VIII	IX	IA	IB	VIII	IX
Sex:	M	M	M	M	F	F	F	F
Rats/Group Examined:	10	10	10	0	10	10	10	0
BONE MARROW:								
NO. EXAMINED	10	10	10	0	10	10	10	0
NO. NORMAL	10	9	3	0	7	9	6	0
-bone marrow hyperplasia,								
very slight	0	0	1	0	1	1	3	0
slight	0	0	4	0	1	0	1	0
moderate	0	0	2	0	0	0	0	0
-focal fibrosis	0	1	0	0	1	0	0	0

*Group IA = Control
Group IB = Control

Group VIII = High-Mid Dose
Group IX = High Dose

RH-6201 and RH-5205
Twenty-four-Month Oral Safety Evaluation Study in Rats
Protocol No. DR-76-3

APPENDIX I
Histopathologic Evaluation of the Bone Marrow
from Control and RH-5205-Treated Rats
67-Day Interim Necropsy

Animal Number: 151-76
Sex: M
Dose Group: Control (Group IB)

BONE MARROW: Very slight hyperplasia of the bone marrow.

Animal Number: 152-76
Sex: M
Dose Group: Control (Group IB)

BONE MARROW: Moderate hyperplasia of the bone marrow.

Animal Number: 153-76
Sex: M
Dose Group: Control (Group IB)

BONE MARROW: Not remarkable.

Animal Number: 154-76
Sex: M
Dose Group: Control (Group IB)

BONE MARROW: Not remarkable.

Animal Number: 155-76
Sex: M
Dose Group: Control (Group IB)

BONE MARROW: Not remarkable.

Animal Number: 1231-76
Sex: M
Dose Group: High RH-5205 (Group IX)

BONE MARROW: Moderate hyperplasia of the bone marrow.

Animal Number: 1233-76
Sex: M
Dose Group: High RH-5205 (Group IX)

BONE MARROW: Marked hyperplasia of the bone marrow.

Animal Number: 1234-76
Sex: M
Dose Group: High RH-5205 (Group IX)

BONE MARROW: Moderate hyperplasia of the bone marrow.

Animal Number: 1235-76
Sex: M
Dose Group: High RH-5205 (Group IX)

BONE MARROW: Marked hyperplasia of the bone marrow.

Animal Number: 1236-76
Sex: M
Dose Group: High RH-5205 (Group IX)

BONE MARROW: Marked hyperplasia of the bone marrow.

Animal Number: 1237-76
Sex: M
Dose Group: High RH-5205 (Group IX)

BONE MARROW: Marked hyperplasia of the bone marrow.

Animal Number: 1238-76
Sex: M
Dose Group: High RH-5205 (Group IX)

BONE MARROW: Marked hyperplasia of the bone marrow and moderate focal areas of myelosclerosis in the diaphysis.

Animal Number: 1239-76
Sex: M
Dose Group: High RH-5205 (Group IX)

BONE MARROW: Moderate hyperplasia of the bone marrow.

Animal Number: 1240-76
Sex: M
Dose Group: High RH-5205 (Group IX)

BONE MARROW: Moderate hyperplasia of the bone marrow.

Animal Number: 1241-76
Sex: M
Dose Group: High RH-5205 (Group IX)

BONE MARROW: Marked hyperplasia of the bone marrow and moderate myelosclerosis in the diaphysis of sternabrae.

RH-6201 and RH-5205
Twenty-four-Month Oral Safety Evaluation Study in Rats
Protocol No. DR-76-3

APPENDIX II
Histopathologic Evaluation of the Bone Marrow
from Control and RH-5205-Treated Rats
80-Day Interim Necropsy

Animal Number: 156-76
Sex: M
Dose Group: Control (Group IB)

BONE MARROW: Very slight hyperplasia of the bone marrow.

Animal Number: 157-76
Sex: M
Dose Group: Control (Group IB)

BONE MARROW: Not remarkable.

Animal Number: 158-76
Sex: M
Dose Group: Control (Group IB)

BONE MARROW: Not remarkable.

Animal Number: 159-76
Sex: M
Dose Group: Control (Group IB)

BONE MARROW: Not remarkable.

Animal Number: 160-76
Sex: M
Dose Group: Control (Group IB)

BONE MARROW: Not remarkable.

Animal Number: 1081-76
Sex: M
Dose Group: High-Mid RH-5205 (Group VIII)

BONE MARROW: Not remarkable.

Animal Number: 1089-76
Sex: M
Dose Group: High-Mid RH-5205 (Group VIII)

BONE MARROW: Moderate hyperplasia of the bone marrow.

Animal Number: 1090-76
Sex: M
Dose Group: High-Mid RH-5205 (Group VIII)

BONE MARROW: Moderate hyperplasia of the bone marrow.

Animal Number: 1091-76
Sex: M
Dose Group: High-Mid RH-5205 (Group VIII)

BONE MARROW: Moderate hyperplasia of the bone marrow.

Animal Number: 1092-76
Sex: M
Dose Group: High-Mid RH-5205 (Group VIII)

BONE MARROW: Slight hyperplasia of the bone marrow.

Animal Number: 1093-76
Sex: M
Dose Group: High-Mid RH-5205 (Group VIII)

BONE MARROW: Moderate hyperplasia of the bone marrow.

RH-6201 and RH-5205
Twenty-four-Month Oral Safety Evaluation Study in Rats
Protocol No. DR-76-3

APPENDIX III
Histopathologic Evaluation of the Bone Marrow
from Control and RH-5205-Treated Rats
90-Day Interim Necropsy

Animal Number: 01-76
Sex: M
Dose Group: Control (Group IA)

BONE MARROW: Not remarkable.

Animal Number: 02-76
Sex: M
Dose Group: Control (Group IA)

BONE MARROW: Not remarkable.

Animal Number: 03-76
Sex: M
Dose Group: Control (Group IA)

BONE MARROW: Not remarkable.

Animal Number: 04-76
Sex: M
Dose Group: Control (Group IA)

BONE MARROW: Moderate hyperplasia of the bone marrow.

Animal Number: 05-76
Sex: M
Dose Group: Control (Group IA)

BONE MARROW: Slight hyperplasia of the bone marrow.

Animal Number: 06-76
Sex: M
Dose Group: Control (Group IA)

BONE MARROW: Not remarkable.

Animal Number: 07-76
Sex: M
Dose Group: Control (Group IA)

BONE MARROW: Not remarkable.

Animal Number: 08-76
Sex: M
Dose Group: Control (Group IA)

BONE MARROW: Not remarkable.

Animal Number: 09-76
Sex: M
Dose Group: Control (Group IA)

BONE MARROW: Not remarkable.

Animal Number: 10-76
Sex: M
Dose Group: Control (Group IA)

BONE MARROW: Not remarkable.

Animal Number: 76-76
Sex: F
Dose Group: Control (Group IA)

BONE MARROW: Slight hyperplasia of the bone marrow.

Animal Number: 77-76
Sex: F
Dose Group: Control (Group IA)

BONE MARROW: Not remarkable.

Animal Number: 78-76
Sex: F
Dose Group: Control (Group IA)

BONE MARROW: Not remarkable.

Animal Number: 79-76
Sex: F
Dose Group: Control (Group IA)

BONE MARROW: Very slight hyperplasia of the bone marrow.

Animal Number: 80-76
Sex: F
Dose Group: Control (Group IA)

BONE MARROW: Not remarkable.

Animal Number: 81-76
Sex: F
Dose Group: Control (Group IA)

BONE MARROW: Not remarkable.

Animal Number: 82-76
Sex: F
Dose Group: Control (Group IA)

BONE MARROW: Not remarkable.

Animal Number: 83-76
Sex: F
Dose Group: Control (Group IA)

BONE MARROW: Not remarkable.

Animal Number: 84-76
Sex: F
Dose Group: Control (Group IA)

BONE MARROW: Very slight hyperplasia of the bone marrow.

Animal Number: 85-76
Sex: F
Dose Group: Control (Group IA)

BONE MARROW: Not remarkable.

Animal Number: 161-76
Sex: M
Dose Group: Control (Group IB)

BONE MARROW: Not remarkable.

Animal Number: 162-76
Sex: M
Dose Group: Control (Group IB)

BONE MARROW: Not remarkable.

Animal Number: 163-76
Sex: M
Dose Group: Control (Group IB)

BONE MARROW: Not remarkable.

Animal Number: 164-76
Sex: M
Dose Group: Control (Group IB)

BONE MARROW: Not remarkable.

Animal Number: 165-76
Sex: M
Dose Group: Control (Group IB)

BONE MARROW: Very slight hyperplasia of the bone marrow.

Animal Number: 226-76
Sex: F
Dose Group: Control (Group IB)

BONE MARROW: Not remarkable.

Animal Number: 227-76
Sex: F
Dose Group: Control (Group IB)

BONE MARROW: Very slight hyperplasia of the bone marrow.

Animal Number: 228-76
Sex: F
Dose Group: Control (Group IB)

BONE MARROW: Slight hyperplasia of the bone marrow.

Animal Number: 229-76
Sex: F
Dose Group: Control (Group IB)

BONE MARROW: Not remarkable.

Animal Number: 230-76
Sex: F
Dose Group: Control (Group IB)

BONE MARROW: Not remarkable.

Animal Number: 231-76
Sex: F
Dose Group: Control (Group IB)

BONE MARROW: Not remarkable.

Animal Number: 232-76
Sex: F
Dose Group: Control (Group IB)

BONE MARROW: Not remarkable.

Animal Number: 233-76
Sex: F
Dose Group: Control (Group IB)

BONE MARROW: Not remarkable.

Animal Number: 234-76
Sex: F
Dose Group: Control (Group IB)

BONE MARROW: Not remarkable.

Animal Number: 235-76
Sex: F
Dose Group: Control (Group IB)

BONE MARROW: Very slight hyperplasia of the bone marrow.

Animal Number: 1232-76
Sex: M
Dose Group: High RH-5205 (Group IX)

BONE MARROW: Moderate hyperplasia of the bone marrow.

Animal Number: 1242-76
Sex: M
Dose Group: High RH-5205 (Group IX)

BONE MARROW: Moderate hyperplasia of the bone marrow.

Animal Number: 1243-76
Sex: M
Dose Group: High RH-5205 (Group IX)

BONE MARROW: Moderate hyperplasia of the bone marrow.

Animal Number: 1244-76
Sex: M
Dose Group: High RH-5205 (Group IX)

BONE MARROW: Marked hyperplasia of the bone marrow.

Animal Number: 1245-76
Sex: M
Dose Group: High RH-5205 (Group IX)

BONE MARROW: Moderate hyperplasia of the bone marrow.

Animal Number: 1246-76
Sex: F
Dose Group: High RH-5205 (Group IX)

BONE MARROW: Moderate hyperplasia of the bone marrow.

Animal Number: 1247-76
Sex: F
Dose Group: High RH-5205 (Group IX)

BONE MARROW: Slight hyperplasia of the bone marrow.

Animal Number: 1248-76
Sex: F
Dose Group: High RH-5205 (Group IX)

BONE MARROW: Not remarkable.

Animal Number: 1249-76
Sex: F
Dose Group: High RH-5205 (Group IX)

BONE MARROW: Not remarkable.

Animal Number: 1250-76
Sex: F
Dose Group: High RH-5205 (Group IX)

BONE MARROW: Very slight hyperplasia of the bone marrow.

Animal Number: 1251-76
Sex: M
Dose Group: High RH-5205 (Group IX)

BONE MARROW: Slight hyperplasia of the bone marrow.

Animal Number: 1252-76
Sex: F
Dose Group: High RH-5205 (Group IX)

BONE MARROW: Very slight hyperplasia of the bone marrow.

Animal Number: 1253-76
Sex: F
Dose Group: High RH-5205 (Group IX)

BONE MARROW: Very slight hyperplasia of the bone marrow.

Animal Number: 1254-76
Sex: F
Dose Group: High RH-5205 (Group IX)

BONE MARROW: Moderate hyperplasia of the bone marrow.

Animal Number: 1255-76
Sex: F
Dose Group: High RH-5205 (Group IX)

BONE MARROW: Moderate hyperplasia of the bone marrow.

Animal Number: 1256-76
Sex: F
Dose Group: High RH-5205 (Group IX)

BONE MARROW: Tissue not available.

RH-6201 and RH-5205
Twenty-four-Month Oral Safety Evaluation Study in Rats
Protocol No. DR-76-3

APPENDIX IV
Histopathologic Evaluation of the Bone Marrow
from Control and RH-5205-Treated Rats
12-Month Interim Necropsy

Animal Number: 16-76
Sex: M
Dose Group: Control (Group IA)

BONE MARROW: Not remarkable.

Animal Number: 17-76
Sex: M
Dose Group: Control (Group IA)

BONE MARROW: Not remarkable.

Animal Number: 19-76
Sex: M
Dose Group: Control (Group IA)

BONE MARROW: Not remarkable.

Animal Number: 20-76
Sex: M
Dose Group: Control (Group IA)

BONE MARROW: Not remarkable.

Animal Number: 21-76
Sex: M
Dose Group: Control (Group IA)

BONE MARROW: Not remarkable.

Animal Number: 22-76
Sex: M
Dose Group: Control (Group IA)

BONE MARROW: Not remarkable.

Animal Number: 23-76
Sex: M
Dose Group: Control (Group IA)

BONE MARROW: Not remarkable.

Animal Number: 24-76
Sex: M
Dose Group: Control (Group IA)

BONE MARROW: Not remarkable.

Animal Number: 25-76
Sex: M
Dose Group: Control (Group IA)

BONE MARROW: Not remarkable.

Animal Number: 26-76
Sex: M
Dose Group: Control (Group IA)

BONE MARROW: Not remarkable.

Animal Number: 91-76
Sex: F
Dose Group: Control (Group IA)

BONE MARROW: Very small focus of fibrosis at the epiphyseal line.

Animal Number: 92-76
Sex: F
Dose Group: Control (Group IA)

BONE MARROW: Very slight hyperplasia of the bone marrow.

Animal Number: 93-76
Sex: F
Dose Group: Control (Group IA)

BONE MARROW: Slight hyperplasia of the bone marrow.

Animal Number: 94-76
Sex: F
Dose Group: Control (Group IA)

BONE MARROW: Not remarkable.

Animal Number: 95-76
Sex: F
Dose Group: Control (Group IA)

BONE MARROW: Not remarkable.

Animal Number: 96-76
Sex: F
Dose Group: Control (Group IA)

BONE MARROW: Not remarkable.

Animal Number: 97-76
Sex: F
Dose Group: Control (Group IA)

BONE MARROW: Not remarkable.

Animal Number: 98-76
Sex: F
Dose Group: Control (Group IA)

BONE MARROW: Not remarkable.

Animal Number: 99-76
Sex: F
Dose Group: Control (Group IA)

BONE MARROW: Not remarkable.

Animal Number: 100-76
Sex: F
Dose Group: Control (Group IA)

BONE MARROW: Not remarkable.

Animal Number: 166-76
Sex: M
Dose Group: Control (Group IB)

BONE MARROW: Not remarkable.

Animal Number: 167-76
Sex: M
Dose Group: Control (Group IB)

BONE MARROW: Not remarkable.

Animal Number: 168-76
Sex: M
Dose Group: Control (Group IB)

BONE MARROW: Not remarkable.

Animal Number: 169-76
Sex: M
Dose Group: Control (Group IB)

BONE MARROW: Not remarkable.

Animal Number: 170-76
Sex: M
Dose Group: Control (Group IB)

BONE MARROW: Not remarkable.

Animal Number: 171-76
Sex: M
Dose Group: Control (Group IB)

BONE MARROW: Marrow is normal, but there is a very small focus of fibrosis at the base of the epiphyseal bone.

Animal Number: 172-76
Sex: M
Dose Group: Control (Group IB)

BONE MARROW: Not remarkable.

Animal Number: 173-76
Sex: M
Dose Group: Control (Group IB)

BONE MARROW: Not remarkable.

Animal Number: 174-76
Sex: M
Dose Group: Control (Group IB)

BONE MARROW: Not remarkable.

Animal Number: 175-76
Sex: M
Dose Group: Control (Group IB)

BONE MARROW: Not remarkable.

Animal Number: 241-76
Sex: F
Dose Group: Control (Group IB)

BONE MARROW: Not remarkable.

Animal Number: 242-76
Sex: F
Dose Group: Control (Group IB)

BONE MARROW: Not remarkable.

Animal Number: 243-76
Sex: F
Dose Group: Control (Group IB)

BONE MARROW: Not remarkable.

Animal Number: 244-76
Sex: F
Dose Group: Control (Group IB)

BONE MARROW: Not remarkable.

Animal Number: 245-76
Sex: F
Dose Group: Control (Group IB)

BONE MARROW: Not remarkable.

Animal Number: 246-76
Sex: F
Dose Group: Control (Group IB)

BONE MARROW: Not remarkable.

Animal Number: 247-76
Sex: F
Dose Group: Control (Group IB)

BONE MARROW: Not remarkable.

Animal Number: 248-76
Sex: F
Dose Group: Control (Group IB)

BONE MARROW: Very slight hyperplasia of the bone marrow.

Animal Number: 249-76
Sex: F
Dose Group: Control (Group IB)

BONE MARROW: Not remarkable.

Animal Number: 250-76
Sex: F
Dose Group: Control (Group IB)

BONE MARROW: Not remarkable.

Animal Number: 1094-76
Sex: M
Dose Group: High-Mid RH-5205 (Group VIII)

BONE MARROW: Not remarkable.

Animal Number: 1095-76
Sex: M
Dose Group: High-Mid RH-5205 (Group VIII)

BONE MARROW: Slight hyperplasia of the bone marrow.

Animal Number: 1096-76
Sex: M
Dose Group: High-Mid RH-5205 (Group VIII)

BONE MARROW: Slight hyperplasia of the bone marrow.

Animal Number: 1097-76
Sex: M
Dose Group: High-Mid RH-5205 (Group VIII)

BONE MARROW: Very slight hyperplasia of the bone marrow.

Animal Number: 1098-76
Sex: M
Dose Group: High-Mid RH-5205 (Group VIII)

BONE MARROW: Moderate hyperplasia of the bone marrow.

Animal Number: 1099-76
Sex: M
Dose Group: High-Mid RH-5205 (Group VIII)

BONE MARROW: Not remarkable.

Animal Number: 1100-76
Sex: M
Dose Group: High-Mid RH-5205 (Group VIII)

BONE MARROW: Moderate hyperplasia of the bone marrow.

Animal Number: 1101-76
Sex: M
Dose Group: High-Mid RH-5205 (Group VIII)

BONE MARROW: Slight hyperplasia of the bone marrow.

Animal Number: 1102-76
Sex: M
Dose Group: High-Mid RH-5205 (Group VIII)

BONE MARROW: Not remarkable.

Animal Number: 1103-76
Sex: M
Dose Group: High-Mid RH-5205 (Group VIII)

BONE MARROW: Slight hyperplasia of the bone marrow.

Animal Number: 1171-76
Sex: F
Dose Group: High-Mid RH-5205 (Group VIII)

BONE MARROW: Not remarkable.

Animal Number: 1172-76
Sex: F
Dose Group: High-Mid RH-5205 (Group VIII)

BONE MARROW: Very slight hyperplasia of the bone marrow.

Animal Number: 1173-76
Sex: F
Dose Group: High-Mid RH-5205 (Group VIII)

BONE MARROW: Very slight hyperplasia of the bone marrow.

Animal Number: 1174-76
Sex: F
Dose Group: High-Mid RH-5205 (Group VIII)

BONE MARROW: Not remarkable.

Animal Number: 1175-76
Sex: F
Dose Group: High-Mid RH-5205 (Group VIII)

BONE MARROW: Very slight hyperplasia of the bone marrow.

Animal Number: 1176-76
Sex: F
Dose Group: High-Mid RH-5205 (Group VIII)

BONE MARROW: Not remarkable.

Animal Number: 1177-76
Sex: F
Dose Group: High-Mid RH-5205 (Group VIII)

BONE MARROW: Slight hyperplasia of the bone marrow.

Animal Number: 1178-76
Sex: F
Dose Group: High-Mid RH-5205 (Group VIII)

BONE MARROW: Not remarkable.

Animal Number: 1179-76
Sex: F
Dose Group: High-Mid RH-5205 (Group VIII)

BONE MARROW: Not remarkable.

Animal Number: 1180-76
Sex: F
Dose Group: High-Mid RH-5205 (Group VIII)

BONE MARROW: Not remarkable.



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

Ronald L. Keener, Ph.D.
Regulatory Affairs Director, Product Integrity Department
Rohm and Haas Company
Independence Mall West
Philadelphia, Pennsylvania 19105

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

APR 10 1995

EPA acknowledges the receipt of information submitted by your organization under Section 8(e) of the Toxic Substances Control Act (TSCA). For your reference, copies of the first page(s) of your submission(s) are enclosed and display the TSCA §8(e) Document Control Number (e.g., SEHQ-00-0000) assigned by EPA to your submission(s). Please cite the assigned 8(e) number when submitting follow-up or supplemental information and refer to the reverse side of this page for "EPA Information Requests".

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Attn: TSCA Section 8(e) Coordinator
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
Washington, D.C. 20460-0001

EPA looks forward to continued cooperation with your organization in its ongoing efforts to evaluate and manage potential risks posed by chemicals to health and the environment.

Sincerely,

Terry R. O'Bryan
Terry R. O'Bryan
Risk Analysis Branch

Enclosure

12252A



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Triage of 8(e) Submissions

SEP 5 1985

Date sent to triage:

NON-CAP

CAP

Submission number: 12252 A

TSCA Inventory:

Y

N

D

Study type (circle appropriate):

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ATOX SBTOX SEN w/NEUR

Group 3 - Elizabeth Margosches (1 copy each)

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STOX/ONCO CTOX/ONCO IMMUNO CYTO NEUR

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entire document 0 1 2 pages 1

pages 1, DMR85

Notes:

Contractor reviewer : POP

Date: 3/21/95

CECATS\TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA:
Submission # 8EHO- 0992-12252 SEQ. A

TYPE: INT. SUPP FLWP

SUBMITTER NAME: Rohm and Haas
Company

SUB. DATE: 07/27/92 OTS DATE: 09/08/92 CSRAD DATE: 02/27/95

INFORMATION REQUESTED: FLWP DATE:

- 0501 NO INFO REQUESTED
 0502 INFO REQUESTED (TECH)
 0503 INFO REQUESTED (VOL ACTIONS)
 0504 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:

- 0639 REFER TO CHEMICAL SCREENING
 0678 CAP NOTICE

VOLUNTARY ACTIONS:

- 0401 NO ACTION REPORTED
 0402 STUDIES PLANNED/UNDERTAKEN
 0403 NOTIFICATION OF WORKERS/EMPLOYERS
 0404 LABEL/MSDS CHANGES
 0405 PROCESS/HANDLING CHANGES
 0406 APP/USE DISCONTINUED
 0407 PRODUCTION DISCONTINUED
 0408 CONFIDENTIAL

CHEMICAL NAME:

Propionic acid, 2-[5-{2-chloro-4-(tri fluoromethyl)-phenoxy}-2-nitrophenoxy]-,
 ethyl ester

CAS#

50594-49-5

INFORMATION TYPE:

P F C

INFORMATION TYPE:

P F C

INFORMATION TYPE:

P F C

0201	ONCO (HUMAN)	01 02 04
0202	ONCO (ANIMAL)	01 02 04
0203	CELL. TRANS (IN VITRO)	01 02 04
0204	MUTA (IN VITRO)	01 02 04
0205	MUTA (IN VIVO)	01 02 04
0206	REPRO/TERATO (HUMAN)	01 02 04
0207	REPRO/TERATO (ANIMAL)	01 02 04
0208	NEURO (HUMAN)	01 02 04
0209	NEURO (ANIMAL)	01 02 04
0210	ACUTE TOX. (HUMAN)	01 02 04
0211	CHR. TOX. (HUMAN)	01 02 04
0212	ACUTE TOX. (ANIMAL)	01 02 04
0213	SUB ACUTE TOX (ANIMAL)	01 02 04
0214	SUB CHRONIC TOX (ANIMAL)	01 02 04
0215	CHRONIC TOX (ANIMAL)	01 02 04

0216	EPI/CLIN	01 02 04
0217	HUMAN EXPOS (PROD CONTAM)	01 02 04
0218	HUMAN EXPOS (ACCIDENTAL)	01 02 04
0219	HUMAN EXPOS (MONITORING)	01 02 04
0220	ECO/AQUA TOX	01 02 04
0221	ENV. OCCC/REL/FATE	01 02 04
0222	EMER INCI OF ENV CONTAM	01 02 04
0223	RESPONSE REQUEST DELAY	01 02 04
0224	PROD/COMP/CHEM ID	01 02 04
0225	REPORTING RATIONALE	01 02 04
0226	CONFIDENTIAL	01 02 04
0227	ALLERG (HUMAN)	01 02 04
0228	ALLERG (ANIMAL)	01 02 04
0239	METAB/PHARMACO (ANIMAL)	01 02 04
0240	METAB/PHARMACO (HUMAN)	01 02 04

0241	IMMUNO (ANIMAL)	01 02 04
0242	IMMUNO (HUMAN)	01 02 04
0243	CHEM/PHYS PROP	01 02 04
0244	CLASTO (IN VITRO)	01 02 04
0245	CLASTO (ANIMAL)	01 02 04
0246	CLASTO (HUMAN)	01 02 04
0247	DNA DAM/REPAIR	01 02 04
0248	PROD/USE/PROC	01 02 04
0251	MSDS	01 02 04
0299	OTHER	01 02 04

TRIAGE DATA: NON-CBI INVENTORY

ONGOING REVIEW

SPECIES

TOXICOLOGICAL CONCERN:

USE:

PRODUCTION:

YES

YES (DROP/REFER)

RAT
MUS

LOW

CAS SR

NO

MED

IN INMINI

HIGH

1000000000

-CPSS-

> <ID NUMBER>
8 (E) -12252A

> <TOX CONCERN>

~~High~~

*STET
MEPIKA*

> <COMMENT>

ONCOGENICITY IN MICE IS OF HIGH CONCERN. IN 2-YEAR CHRONIC STUDY OF MICE, ORAL DOSES OF 0.1, 0.32 AND 1.0-0.7 MG/KG EACH ADMINISTERED ORALLY TO GROUPS OF MALE AND FEMALE MICE (78-80/SEX/GROUP) WERE ASSOCIATED WITH SIGNIFICANTLY INCREASED MORTALITY DURING MONTHS 1-3 OF TREATMENT ONLY AT THE HIGH DOSAGE (1.0-0.7 MG/KG) AND INCREASED INCIDENCE OF LIVER NODULES AND MASSES AT ALL DIETARY REGIMENS. TUMORS WERE IDENTIFIED IN DECEDENT ANIMALS FROM 13 MONTHS AND SURVIVING ANIMALS AT TERMINAL 24TH MONTH SACRIFICE, AND THE CARCINOGENIC EFFECT TO THE LIVER WAS MOST PRONOUNCED AT LOW (63%M, 36.5%F) AND MEDIUM (65.4%M, 29.6%F) DOSAGES AND AMONG MALE ANIMALS.

Low
ONCOGENICITY IN RATS IS OF HIGH CONCERN. IN 2-YEAR CHRONIC STUDY OF RATS, DIETARY CONCENTRATIONS DESIGNATED AS LOW, LOW-MID, HIGH-MID AND HIGH WERE ADMINISTERED TO GROUPS OF MALE AND FEMALE RATS AS FOLLOWS: 1, 1,4 AND 2 PPM FOR WEEKS 1-2, 3-4 AND DAYS 29-90+ RESPECTIVELY IN THE LOW GROUP (75/SEX/GROUP); 3,15, 4.45 AND 6.3 PPM FOR WEEKS 1-2, 3-4 AND DAYS 29-90+ RESPECTIVELY IN THE LOW-MID GROUP (75/SEX/GROUP); 10, 14.1, 20 AND 11.9 PPM FOR WEEKS 1-2, 3-4, DAYS 29-79 AND DAYS 90+ IN THE FEMALE HIGH-MID GROUP (75 FEMALES/GROUP); 10, 14.1, 20 PPM FOR WEEKS 1-2, 3-4 AND DAYS 29-90+ RESPECTIVELY IN THE MALE HIGH-MID GROUP (75 MALES/GROUP); 31.5, 44.5 AND 63 PPM FOR WEEKS 1-2, 3-4 AND DAYS 29-67 IN THE FEMALE HIGH GROUP (15 FEMALES/GROUP); 31.5, 44.5 AND 63 PPM FOR WEEKS 1-2, 3-4 AND DAYS 29-90 RESPECTIVELY IN THE MALE HIGH GROUP (75 MALES/GROUP). REPORT OF MICROSCOPIC EXAMINATION OF HEMATOXYLIN-AND-EOSIN-STAINED SECTIONS OF BONE AND BONE MARROW ONLY FOLLOWING 2-YEAR ONCOGENICITY (CHRONIC ORAL EXPOSURE) STUDY IN RATS DOCUMENTED MODERATE TO MARKED HYPERPLASIA OF THE BONE MARROW IN 10/10 HIGH-DOSE (63 PPM) MALE ANIMALS RELATIVE TO SLIGHT TO MODERATE HYPERPLASIA IN 2/5 MALE CONTROL ANIMALS AT 67TH DAY NECROPSY OF 10 MALE HIGH-DOSE AND 5 MALE CONTROL RATS; FOCAL MYELOSCLEROSIS WAS ALSO IDENTIFIED IN 2/10 AND 1/10 OF THESE HIGH-DOSE AND CONTROL MALES RESPECTIVELY. TREATMENT-RELATED INCIDENCE OF BONE MARROW HYPERPLASIA AND FOCAL MYELOSCLEROSIS RESPECTIVELY WERE ALSO DEMONSTRATED UPON 80TH DAY NECROPSY OF 13 HIGH-MID DOSE (10-20 PPM) MALES (12/13, 1/13), 90TH DAY NECROPSY OF HIGH-DOSE (63 PPM) MALES (5/6, 1/6) AND FEMALES (7/9, 0/9) AND 12TH MONTH NECROPSY OF HIGH-MID DOSE (10-20 PPM) MALES (7/10, 0/10) AND FEMALES (4/10, 0/10).

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